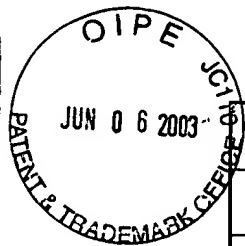


06-09-03

GAU-1639



AMENDMENT TRANSMITTAL LETTER

Docket No.
RGV-003

RECEIVED

Application No.
09/712821Filing Date
November 13, 2000Examiner
Ponnaluri, PadmashriArt Unit
1639

JUN 11 2003

Applicant(s): Todd M. Kinsella

Invention: METHODS AND COMPOSITIONS FOR SCREENING USING DIPHTHERIA TOXIN
CONSTRUCTS

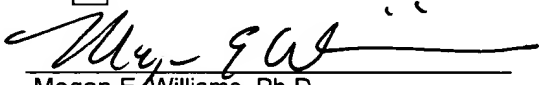
TECH CENTER 1600/2900

TO THE COMMISSIONER FOR PATENTS

Transmitted herewith is an Amendment and Response to the Office Action (8 pages) in the above-identified application, including a return receipt postcard.

The fee has been calculated and is transmitted as shown below.

CLAIMS AS AMENDED					
	Claims Remaining After Amendment	Highest Number Previously Paid	Number Extra Claims Present	Rate	
Total Claims	50	- 50 =		x	0.00
Independent Claims	5	- 7 =		x	0.00
Multiple Dependent Claims (check if applicable) <input type="checkbox"/>					
Other fee (please specify):					
TOTAL ADDITIONAL FEE FOR THIS AMENDMENT:					0.00

☒ Large Entity☐ Small Entity☒ No additional fee is required for this amendment.☐ Please charge Deposit Account No. _____ in the amount of \$ _____.
A duplicate copy of this sheet is enclosed.☐ A check in the amount of \$ _____ to cover the filing fee is enclosed.☐ Payment by credit card. Form PTO-2038 is attached.☒ The Director is hereby authorized to charge and credit Deposit Account No. 12-0080
as described below. A duplicate copy of this sheet is enclosed.☒ Credit any overpayment.☒ Charge any additional filing or application processing fees required under 37 CFR 1.16 and 1.17.

 Megan E. Williams, Ph.D.
 Attorney Reg. No.: 43,270

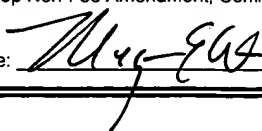
Dated: June 6, 2003

 LAHIVE & COCKFIELD, LLP
 28 State Street
 Boston, Massachusetts 02109
 (617) 227-7400

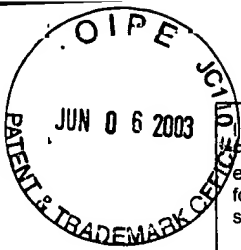
 I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV 355 388 146
 US, in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-
 1450, on the date shown below.

Dated: June 6, 2003

Signature:



(Megan E. Williams, Ph.D.)



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Dated: June 6, 2003

Signature:

Megan E. Williams
(Megan E. Williams)

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JUN 11 2003

TECH CENTER 1600/2900 Docket No.: RGV-003
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Todd M. Kinsella

Application No.: 09/712,821

Group Art Unit: 1639

Filed: November 13, 2000

Examiner: Ponnaluri, Padmashri

For: Methods and Compositions for Screening Using
Diphtheria Toxin Constructs

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

#19
150998
6-19-03

AMENDMENT AND RESPONSE TO OFFICE ACTION

Dear Sir:

This is in response to the Office Action dated May 6, 2003 (Paper No. 18).

REMARKS

Claims 13-45 remain pending and are presently under examination. For the Examiner's convenience, the pending claims are set forth in Appendix A.

The Examiner is of the opinion that "[t]he reply filed on 2/5/03, paper number 17, is not fully responsive to the prior Office action." In particular, the Examiner has stated that

Applicants in the response to the election of species stated the '2a site and the IRES site are both species of sites which allow for separation of the two selection genes'. And applicants have elected '2a site' as the site for separation of two selection genes. However, the elected independent claim 21 recites that the vector comprises IRES site, which is not the elected species. None of the elected group II claims read on the elected species.

Applicants respectfully request that the previous species election of the 2a site which was made in the previous Response (Paper No. 17), be vacated. Applicants hereby elect, under 35 U.S.C. 121, the species of **CD9** for search purposes only. Based on the new species election of CD9, as set forth herein, it is Applicants' understanding that they have been fully responsive to the Restriction Requirement.

The Examiner is also of the opinion that

Applicants have elected GFP as the species of additional selection gene. However, the elected claims recite that the vector comprises first and second selection gene, and the first or second selection gene is HBEGF gene. Amended claim 22 recites that the vector further comprises an additional selection gene. That means the vectors according to claim 22 has 3 selection genes. Applicants have elected GFP as a selection gene, and HBEGF is the other selection gene, it is not clear whether the 3rd selection gene is present, and if present what is the location of the 3rd selection gene, and what would read on the 3rd selection gene.

Applicants respectfully submit that claim 21 is directed to an expression vector comprising a first and a second selection gene which are fused such that transcription from a promoter operably linked to the first selection gene results in a single transcript encoding the first and second selection genes and further comprising an IRES site interposed between the first and second selection genes. The first or second selection gene is an HBEGF gene. Claim 22 is directed to the vector of claim 21, further comprising an additional selection gene, *e.g.*, a third selection gene. Applicants respectfully submit that it is clear that a third selection gene is present in the embodiment of claim 22.

Applicants' specification at page 7, line 27, defines a selection gene, or reporter gene, as "a gene that by its presence in a cell (*i.e.* upon expression) can allow the cell to be distinguished into from a cell that does not contain the reporter gene. Reporter genes can be classified into several different types, including detection genes, survival genes, death genes and cell cycle genes." Moreover, at page 22, lines 24-29, Applicants' specification teaches that suitable selection genes include, but are not limited to "neomycin, blastocidin, bleomycin, puromycin, and hygromycin resistance genes, as well as self-fluorescent markers such as green fluorescent protein, enzymatic markers such as lacZ, and surface proteins such as CD8." For purposes of being responsive to the previous Office Action (Paper No. 16), Applicants have elected, under 35

U.S.C. 121, **GFP** as the species of additional selection gene. However, Applicants respectfully submit that the claims should not be limited to the use of only two selection genes. Applicants' specification describes the use of more than two selection genes in the constructs of the claimed invention. For example, at page 14, lines 15-18, Applicants' specification teaches that "[i]n addition to the promoter of interest, such as an IL-4 inducible ϵ promoter and reporter gene, the fusion nucleic acids may comprise additional components, including, but not limited to, other reporter genes, protein cleavage sites, internal ribosome entry sites (IRES)...". Furthermore, Figure 18 of Applicants' specification clearly depicts a variety of constructs, including constructs comprising three selection genes, e.g., HBEGF, GFP and puromycin (see Figure 18 D, for example). Moreover, dependent claim 32 indicates that the additional selection gene may be a drug resistance gene conferring resistance to drugs selected from the group consisting of puromycin, neomycin, blastocidin, bleomycin, and hygromycin.


Accordingly, for the reasons set forth above, Applicant's respectfully submit that it is clear that there may be a third selection gene present in a construct of the invention as claimed, e.g., in claim 22. Moreover, as set forth above, Applicants specification teaches possible locations of a third selection gene and exemplary species of third selection genes. Applicants' respectfully submit that the claims should not be limited to constructs comprising one or two selection genes based on the teachings of Applicants' specification. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the statement that the previous Response (Paper No. 17) was not fully responsive, and, if necessary, issue a second Restriction Requirement with an amended species election requirement to clarify the record regarding the species of selection genes.

CONCLUSION

In view of the amendments set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: **June 6, 2003**

Respectfully submitted,

By 
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